IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Neil H. Bander
Serial No. : 09/357,709
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Title : TREATMENT AND DIAGNOSIS OF PROSTATE CANCER

Art Unit : 1642
Examiner : Gary Nickol

Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 CFR 1.131

I, Neil H. Bander, a citizen of the United States, residing at 2 Hemlock Hills, Chappaqua, NY, 10514, hereby declare as follows:

1. I am the inventor of the subject matter disclosed and claimed in the above-referenced United States Patent Application.

2. I am familiar with the present claims of the application, which are directed to a method of detecting normal, benign hyperplastic, or cancerous prostate cells or a portion thereof in a human subject.

3. Prior to March 25, 1996, I had completed my invention as described and claimed in the above-identified application in this country, a NAFTA country or WTO country, as evidenced below.

4. I submit herewith Exhibits A-L, evidence showing conception and reduction to practice of the claimed invention prior to the March 25, 1996.

Prior to March 25, 1996, I had conceived of using monoclonal antibodies in the treatment and detection (e.g., imaging) of prostate cancer in humans.

Exhibit A shows an excerpt from a document describing my research on antibodies and their use in cancer that I wrote prior to March 25, 1996. The document dates, dates within the text of the document, and the name of the individual to whom the document is addressed, have been redacted in the excerpt

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR §1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

10-9-02
Date of Deposit

Roberta L. Hahn
Signature

Roberta L. Hahn
Typed or Printed Name of Person Signing Certificate

provided in Exhibit A. The document clearly demonstrates that I was interested in and actively pursuing monoclonal antibodies for clinical, e.g., diagnostic, use in prostate cancer.

As indicated in that document, my laboratory had been testing several monoclonal antibodies for their ability to bind to live LNCaP cells, a human prostate cancer model cell line. Several of the antibodies I had already characterized had demonstrated excellent potential, in that they were able to lyse LNCaP cells *in vitro* in the presence of human serum as a source of complement. More importantly, I had demonstrated that the antibodies were useful for detecting both prostate cancer and sites of metastatic disease (in the lymph nodes and liver). For example, I reported that some of these antibodies had been used to image prostate cells and known sites of metastatic disease. Exhibit A does not discuss the specific antibodies of the invention. In connection with the work described in Exhibit A, I characterized other monoclonal antibodies including the antibodies of the invention. This is shown in Exhibits B-L below.

Exhibit B, is a tag from a mouse cage in my (Dr. Bander's) laboratory indicating that mice immunized with LNCaP cells as part of "Fusion E" experiments were received, immunized, and given a final booster. Dates on the tag have been redacted. The dates show the work was done prior to March 25, 1996.

Exhibits C-L discussed below all show pages from notebooks from my (Dr. Bander's) laboratory. The dates on each of the pages is redacted. Each page is dated prior to March 25, 1996.

Exhibit C is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry shows rosette and cytotoxicity studies of the fusion E antibodies including monoclonal antibody E99 (which is an antibody of the invention), and demonstrates that monoclonal antibody E99 binds to LNCaP cells, a human prostate cancer cell line.

Exhibit D is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that E99 binds renal tubules very weakly, and binds prostate cancer cells strongly.

Exhibit E is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that E99 binds to benign hyperplastic prostate tissue obtained from various human patients. E99 was detected using a fluorescein label.

Exhibit F is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that E99 is an IgG_3 class antibody.

Exhibit G is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that the E99 antibody is capable of lysing PSMA-expressing LNCaP cells, but not PSMA-negative PC3 and Du145 cells.

Exhibit H is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that E99 binds strongly to prostate cancer and benign hyperplastic prostate tissues from human patients, binds normal kidney proximal tubules weakly, and does not bind at all to normal liver, lung, pancreas, testis, esophagus, uterus, small bowel, stomach, thyroid, or spleen.

Exhibit I is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that E99, J415 and J533 (all of which are antibodies of the invention) bind kidney proximal tubules and LNCaP prostate cancer cells, a human prostate cancer cell line, but do not bind normal colon.

Exhibit J is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that E99 and J591 (both of which are antibodies of the invention) bind kidney proximal tubules and LNCaP prostate cancer cells, but do not bind normal colon.

Exhibit K is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates that the J415, J533, and E99 antibodies bind weakly to proximal tubule cells of the normal kidney, and bind benign hyperplastic prostate and cancerous prostate tissue from human patients, and that the J415 and J533 antibodies do not bind at all to normal liver, small intestine, or lung.

Exhibit L is an entry from a laboratory notebook in my (Dr. Bander's) laboratory. This entry demonstrates monoclonal antibodies including E99, J415, J533 and J591 bind to prostate cancer tissue from a number of individuals.

5. Exhibit A demonstrates that I had conceived of using monocolonal antibodies in the detecting of prostate cancer and Exhibits B-L demonstrate that antibodies which bind PSMA and recognize benign hyperplastic, and cancerous prostate cells from human patients were produced for use in detection prior to March 25, 1996. In sum, I submit evidence herewith that shows conception and reduction to practice of the claimed invention prior to March 25, 1996.

6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, under Title 18 § 1001 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

10/7/02
Date

Neil Bander, MD